SYNLETT Spotlight 305

Ethyl 2-Cyano-3,3-bis(methylthio)acrylate

Compiled by Mohan Balasaheb Kalyankar

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Mohan Balasaheb Kalyankar was born in Kharabi, Nanded, India in 1983. He completed his B.Sc. and M.Sc. from Yeshwant Mahavidyalaya Nanded affiliated to S. R. T. M. University, Nanded, India. Currently he is carrying out his Ph.D. in the Department of Organic Chemistry, North Maharashtra University, Jalgaon, India under the supervision of Dr. S. V. Bhosale. His research interests include the synthesis and self-assembly of porphyrins with particular emphasis on the fabrication of soft material via self-assembly.

Department of Organic Chemistry, North Maharashtra University, Jalgaon-425001, India

E-mail: kalyankar.mb@rediffmail.com

Dedicated to my father late B. M. Kalyankar and dedicated to my supervisor Dr. S. V. Bhosale (Reader) on the occasion of his 37th birthday.

Introduction

Ethyl 2-cyano-3,3-bis(methylthio)acrylate (Figure 1) was prepared by the reaction of ethyl cyanoacetate, carbon disulfide and dimethyl sulfate in the presence of a base.¹ Gompper and co-workers studied this reaction thoroughly. The electron-attracting groups on C₂ makes it a very useful reagent for the preparation of heterocyclic com-

pounds.² Moreover, Ethyl 2-cyano-3,3-bis(methylthio)acrylate can also be prepared efficiently using sodium ethoxide as a base.³ In the literature numerous reports appeared highlighting its chemistry and use.

Figure 1 Ethyl 2-Cyano-3,3-bis(methylthio)acrylate

Abstracts

(A) Tominaga et al. reported the synthesis of 2*H*-pyran-2-one starting from acetophenones and ethyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of KOH in DMF.⁴

(B) The 2*H*-pyran-2-one derivatives have been prepared by reacting an aryl methyl ketone and 1,2-diarylethanone with methyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of KOH in DMF.⁵

(C) Baheti et al. described the synthesis of 4*H*-pyrimido[2,1-*b*]benzothiazole-8-substituted 2-thiomethyl-3-cyano-4-ones by the reaction of 2-amino-6-substituted benzothiazole with ethyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of anhydrous potassium carbonate in DMF.⁶ The synthesized compounds were further investigated for analgesic and CNS-depressant activity.

(D) Recently, the group of V. J. Ram described the synthesis of 4-methylsulfanyl-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles by the reaction between 1-tetralone and methyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of KOH/DMSO in catalytic amounts.⁷

(E) The condensation reaction between ethyl 2-cyano-3,3-bis(methylthio)acrylate and alkyl 2-mercaptoacetate leading to highly functionalized thiophenes was reported by V. J. Ram and co-workers.⁸

(F) Suitably functionalized pyrimidine derivatives were synthesized by condensation of ethyl 2-cyano-3,3-dimethylthioacrylate with amidine.⁹ Kohara and co-workers also synthesized pyrimidine derivatives starting from ketene dithioacetal and amides in the presence of sodium hydride in DMA.⁹

(G) Mukharjee et al. reported the synthesis of pyridopyrimidine starting from cyanoketene dithioacetal and 2-aminopyridine in the presence of triethylamine in benzene.¹⁰

(H) The synthesis of triazepines was described by Omran et al. by condensation of *N,N'*-diphenylpiperidine-1-carbohydrazonamide with ethyl 2-cyano-3,3-dimethylthioacrylate in the presence of *t*-BuOH and TEA.¹¹

(I) Yang and co-workers describe the synthesis of 3-aryl-5-cyano-6-methylthio pyrimidine-2,4-diones from ethyl 2-cyano-3,3-dimethylthioacrylate with arylureas in toluene and DMA under mild condition.¹²

(J) Novel ketene N,S-acetals were prepared by the reaction of ethyl 2-cyano-3,3-bis(methylthio)acrylate with low nucleophilic aromatic amines using sodium hydride in toluene.¹³

(K) Metwally and co-workers described the reaction of ethyl 2-cyano-3,3-bis(methylthio)acrylate with aminoazoles (5-aminotetrazole monohydrate and 2-aminothiazole) in the presence or absence of triethylamine leading to the corresponding pyrimidines.¹⁴

References

- Gompper, R.; Topfl, W. *Chem. Ber.* **1962**, *95*, 2861.
- (a) Chauhan, S. M. S.; Junjappa, H. *Tetrahedron* **1976**, *32*, 1779. (b) Chauhan, S. M. S.; Junjappa, H. *Tetrahedron* **1976**, *32*, 1911. (c) Potts, K. T.; Cipullo, M. J.; Ralli, P.; Theodoridis, G. *J. Am. Chem. Soc.* **1981**, *103*, 3584. (d) Kumar, A.; Mhatra, S.; Ila, H.; Junjappa, H. *J. Chem. Soc. Chem. Commun.* **1976**, 592.
- Kumar, A.; Malhotra, S.; Vats, A.; Himanashu; Singh, S. K.; Sharma, S. K.; Prasad, A. K.; Errington, W.; Olsen, C. E.; Jain, S. C.; Parmar, V. S. *Indian J. Chem.* **2002**, *41B*, 360.
- Tominaga, Y.; Ushirogouchi, A.; Matsuda, Y.; Kobayashi, G. *Chem. Pharm. Bull.* **1984**, *32*, 3384.
- (a) Ram, V. J.; Verma, M. *Indian J. Chem.* **1990**, *29B*, 624. (b) Pratap, R.; Kumar, B.; Ram, V. J. *Tetrahedron* **2007**, *63*, 10300. (c) Singh, F. V.; Vatsyayan, R.; Roy, U.; Goel, A. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2734.
- Baheti, K. G.; Kuberkar, S. V. *Indian J. Heterocycl. Chem.* **2003**, *12*, 343.
- (a) Pratap, R.; Ram, V. J. *Tetrahedron Lett.* **2007**, *48*, 4715. (b) Pratap, R.; Ram, V. J. *J. Org. Chem.* **2007**, *72*, 7402.
- Ram, V. J.; Goel, A.; Shukla, P. K.; Kapil, A. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 3101.
- (a) Agarwal, N.; Raghuwanshi, S. K.; Upadhyay, D. N.; Shukla, P. K.; Ram, V. J. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 703. (b) Kohra, S.; Tominaga, Y.; Hosomi, A. *J. Heterocycl. Chem.* **1988**, *25*, 959.
- Mukherjee-Singh, O.; Farooque, M. A. *Indian J. Chem.* **2004**, *43B*, 1561.
- Omran, O. A.; Amer, A. A.; Khodairy, A. *Synth. Commun.* **2006**, *36*, 3647.
- Liu, H.; Yang, G.; Chen, K.; Yang, H. *Synth. Commun.* **1999**, *29*, 3143.
- Liu, H.; Lu, R.; Yang, H. *Synth. Commun.* **1998**, *28*, 3965.
- Metwally, M. A.; Desoky, E. I.; Fawzy, R.; Etman, H. A. *Chem. Heterocycl. Compd.* **2007**, *43*, 382.